

NITRIC OXIDE BASED THERAPEUTICS FOR THE TREATMENT OF LUNG CANCER

SUMMARY

The National Cancer Institute's Chemical Biology Laboratory seeks partners interested in collaborative research to co-develop nitric oxide (NO) based prodrugs for the treatment of lung cancer.

REFERENCE NUMBER

E-025-2010

PRODUCT TYPE

- Therapeutics

KEYWORDS

- nitric oxide
- NO
- reactive oxygen species
- ROS
- diazeniumdiolate
- prodrug

COLLABORATION OPPORTUNITY

This invention is available for licensing.

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DESCRIPTION OF TECHNOLOGY

Nitric oxide (NO) has a broad spectrum of actions in physiological and pathological processes. NO-donor drugs have shown therapeutic effect in several cancer types by inducing apoptosis but the concentrations required have suggested limited clinical applicability. For cancers such as non-small cell lung cancer where most therapies are not curative, there remains a need for effective treatments.

Scientists at the National Cancer Institute have identified a diazeniumdiolate-based NO releasing prodrug, JS-36-25, with selective cytotoxicity towards cancer cells. This prodrug has potent tumoristatic activity in lung cancer cells *in vitro* and in mice xenografts. Treatment with JS-36-25 *in vivo* led to 85% reduction of tumor growth. The tumoristatic potency of the compound had a negative correlation with the level of endogenous reactive oxygen species (ROS) in the cancer cells. Thus, in addition to potent

tumoristatic activity when administered alone, this compound is predicted to have a strong synergy with therapeutics that act through generation of ROS, such as bortezomib, doxorubicin, as well as high-energy radiation.

POTENTIAL COMMERCIAL APPLICATIONS

- Could be used as a stand-alone therapy or in combination with currently available therapeutics

COMPETITIVE ADVANTAGES

- Potent tumoristatic activity with selective cytotoxicity for cancer cells over normal cells
- Demonstrated 85% reduction of tumor growth *in vivo*
- Predicted synergy with other therapeutics

INVENTOR(S)

Larry Keefer (NCI)

DEVELOPMENT STAGE

- Pre-clinical (in vivo)

PUBLICATIONS

1. Maciag, A.E., *et al.* *JPET*, 2011 [PMID: [20962031](#)]
2. Maciag, A.E., *et al.* *J Med Chem*, 2011 [PMID: [22003962](#)]
3. Nandurdikar, R.S., *et al.* *Biorg Med Chem*, 2012 [PMID: [22480849](#)]

PATENT STATUS

- **U.S. Filed:** PCT Application No. PCT/US2012/060785 filed 18 Oct 2012

THERAPEUTIC AREA

- Cancer/Neoplasm